F16. 14.

E D G S K Y E T I H D T E E P A K D M H D A S D S TTGAGTGGAAAGTCTCAGCATCTGAGAGTGGGCCTGGTTCCCAACAATCTCAGACTTTGAGGATAATAC) E W K D G A S P S E S G P G S Q I S D F E D N T SGTCTGATGAGTCTTCCCAGAGTGAAGATGCAAGAGAGCAGTAAGCCAGCTGCCAAAAAAAA	AGARGCAGCAAGCAGCTGTTTCCAACAAATCTCAGACTTTGAGGATAATACATGT L D G A S P S E S G P G S Q I S D F E D N T C AGATGTCCCAAAGTGAAGATGCAAGGAGCCTGGTTCCCAACAAAATCTCCAAAAAAATGCAAGATACATGT S S Q S E D A R S S K P A A K K A T V Q D D CCTATGGAAAAGTTGAAGGGTTTTGGTCCAAGGACCAGTGGGAAATGCAAGATGCAGG Y G K V E G F W S K D Q S Q W E N A E CAAATAGCAAATGAAGAGTTTTGGTCCAAGGACCAGTGAAAGCAAAAGCAAATGAAATGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAA	E E E E E E E E E E E E D G S K Y E T I H L T E E P A K L M H D A S D S E 660 1981 GTAGACCAAGATGACTGAAGATGAAGATGCTTCACATCTGAGGCTGGTTCCCAACAATCTCAGACTTTGAGGATAATACATGT V D Q D D V V E W K D G A S P S E S G P G S Q I S D F E D N T C 693 2080 GAATGAAACCAGGACCTGGTCTGATGAGGTGAAGATGCAAGGACCAGCTGCCAAAAAAAGGTTACAGTGCAAGATGACAGTGCAAGATGACAGTGAAGATGAAAAGTTGAAAAGTTGAAGAGCAGTTTTGGTCCAAGGACCAGTGGGAAAATGCAAGAATGATTGAAAAGTTGAAGAGCTATTGGTCCAAGGACCAGTCACAGTGGGAAAATGCAAATGCAAATTGAAAAGTTGAAGAGGAGTTTTGGTCCAAGGGCAGTTTGACAAGTTGAAAATGCAAATTGACAATTGACAATTGACAAGTGGGAAAATGACAAATTGACAATTGACAAGTGAGGAGAGATTGACAATTGACAATTGACAATTGACAAGTGGGAAATTGACAATTGACAATTGACAAGTGGGAAATTGACAATTGACAATTGACAAGTGGGAAATTGACAATTGACAATTGACAAGTTGACAAGTGAGGAGATTGACAATTGACAATTGACAATTGACAAGTGGGAAATTGACAATTGACAAGTGAGGAGAGTTTGACAGAATGACTGAGGAGTTGACTGAC
EWKDOG ASPESSON DE CONTROLL OF THE CONTROLL OF	TO GO A STATEMENT OF THE STATEMENT OF TH	TO SEE SO TO SEE SO TO SEE SOUTH TO SEE SEE SEE SEE SEE SEE SEE SEE SEE SE
GGICTGATGAGICTTCCCAGAGIGAAGATGCAAGGAGCAGTAAGCCAGCTGCCAAAAAAAAGGCTACAGTGCAAAAA S D E S S Q S E D A R S S K P A K K K A T V Q D AGAATAGTTCCTATGGAAAAGTTGAAGGGTTTTGGTCCAAGGACCAGTCACAGTGGGAAAATGCATCTGAGAATGC N S S Y G K V E G F W S K D Q S Q W E N A S E N A TTGAGTGGCAGAATAGCACAATTGACAGTGAGGAGGAGCAGTTTGACAGCATGACTGAGGAGTTGCTGATCC TTGAGTGGCAGAATAGCACAATTGACAGTGAGGAGCAGTTTGACAGCATGACTGAC	AGTCTTCCCAGAGTGAAGATGCAAGGAGCAGTAAGCCAAAAAAAA	TGAAGATGCAAGGAGCAGCTGCCAAAAAAAAAGGCTACAGTGCAAGATGAC E D A R S S K P A A K K K A T V Q D D TGAAGGGTTTTGGTCCAAGGACCAGTCACAGTGGGAAAATGCATCTGAGAATGCAGAG E G F W S K D Q S Q W E N A S E TGACAGTGAGGGGGGGGGGGTTTGACAGCATGTGGGGGGGG
S D E S S Q S E D A R S S K P A A K K K A T V Q D AGAATAGTTCCTATGGAAAAGTTGAAGGGTTTTGGTCCAAGGACCAGTCACAGTGGGAAAATGCATCTGAGAATGCJAAATGCATGAGAATGCATTTGACAGTGGGAAAATGCATCAGAGAATGACAGTGACAGTGACAGTTGACAGTTGACAGTGACGGGAGTTGACAGTTGACAGTTGACAGTTGACAGTTGACAGTTGACAGTGACGGAGTTGCTGATCCCGATGACTGAC	S S Q S E D A R S S K P A A K K A T V Q D D CCTATGGAAAGTTGAGAGGGTTTTGGTCCAAGGACCAGTCACAGTGGGAAAATGCATCTGAGAATGCAGGGGGGGG	E D A R S S K P A A K K K A T V Q D D TGAAGGGTTTTGGTCCAAGGACCAGTCACAGTGGGAAAATGCATCTGAGAATGCAGAG E G F W S K D Q S Q W E N A S E N A E TGACAGTGAGGAGGAGCAGTTTGACAGCATGACGGAGTTGCTGATCCCATG D S E D G E Q F D S M T D G V A D P M CTGA
AGAATAGTTCCTATGGAAAGGTTGAAGGGTTTTGGTCCAAGGACCAGTCACAGTGGGAAAATGCATCTGAGAATGC) N S S Y G K V E G F W S K D Q S Q W E N A S E N A F T A S E T A S T T TGAGTGGGAGGGGGGGGGGGGGGGGGGGG	CCTATGGAAAAGTTGAAGGGTTTTGGTCCAAGGACCAGTGCGGAAAATGCATCTGAGAATGCAGGAGGGGGGGG	TGAAGGGTTTTGGTCCAAGGACCAGTCACAGTGGGAAAATGCATCTGAGAATGCAGAG E G F W S K D Q S Q W E N A S E N A E S S S S S S S S S S S S S S S S S S
N S S Y G K V E G F W S K D Q S Q W E N A S E N A TIGAGTGGCAGATAGCACATTGACAGTGAGGGGGAGCAGTTTGACAGCATGACTGAC	Y G K V E G F W S K D Q S Q W E N A S E N A E NAATAGAATAGCACAATTGACAGGGGGGGGGGGGGGGGGG	EGFWSKDQSQWE <u>NAS</u> ENABE TGACAGTGAGGAGCAGTTTGACAGCATGACGGAGTTGCTGATCCCATG DSEDGEQGAGCAGTTTGACAGCATGACGGAGTTGCTGATCCCATG CTGA
TGAGTGGCAGAATAGCACAATTGACAGTGAGGAGGAGCAGTTTGACAGCATGACGGAGTTGCTGATCC E W Q <u>N S T</u> I D S E D G E Q F D S M T D G V A D P	ROBATAGCACAATTGACAGTGAGGAGGAGCAGTTTGACAGCATGACGGAGTTGCTGATCCCATG N S T I D S E D G E Q F D S M T D G V A D P M GCAGCCAGCAAGCTGA S Q Q A *	TGACAGTGAGGAGGAGCAGTTTGACAGCATGACTGACGGAGTTGCTGATCCCATG DSEDGEQFDSMTTGACAGCATGACTGAGGAGTTGCTGATCCCATG CTGA
EWQNSTIDSEDGEQFDSMTDGVADP	N S T I D S E D G E Q F D S M T D G V A D P M GCAGCCAGCAAGCCTGA	DSEDGEQFDSMTDGVADPM CTGA
	GCAGCCAGCAAGCCTGA	CTGA *
<u> </u>	* 4 0 0 5	*
HGSLTGVKLSSQQA*		

Double Underline - Glycosilation site (amino acid no. 96-98, 183-185, 371-373, 404-406, 554-556, 584-586, 734-Single Underline - homologies to HSP60 of ADNP Dotted Underline - homologies to PIF1 of ADNP 736, 753-755, 770-772) Bold + Italic - represents two motifs:

1. Glutaredoxin active site (amino acid no. 211-221) 2. Zinc finger C2h2 type, domain (amino acid no. 211-232)

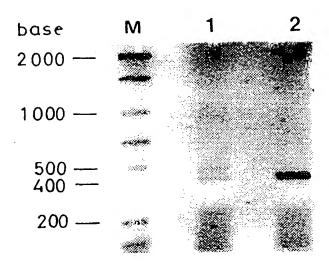


FIG. 2.

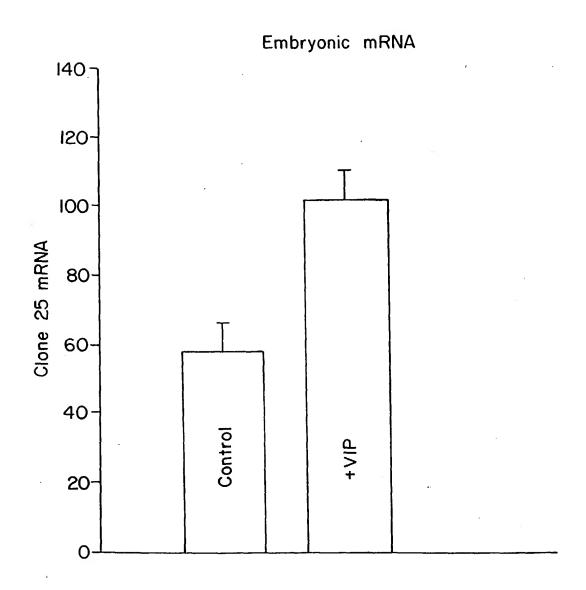


FIG. 3

5/3|

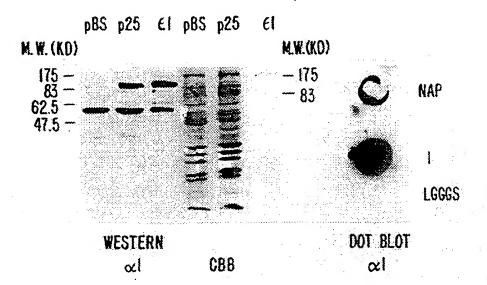
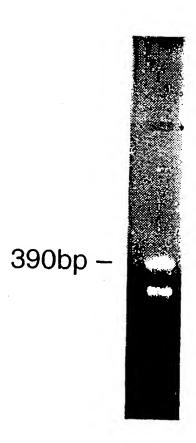


FIG. 4A.

VIP	EXTRACELLULAR:	
M.W.(KD) - 144 87	VIP M.W.(KD) - + -+ 175 - 83 - 52.5 - 47.5 -	VIP M.W.(KD) + + 175 - 83 - 62.5 - 47.5 -
32.7 —	16.5	32.5 - 25 - 6.5 = 6.5
αΙ		WE WIL

FIG. 4B.



Neuroblastoma (NMB)

FIG. 5A.

SENSE

8/31

,	CATTGGGCCG	ACGTCGCATG	CTCCCGCCG	CCATGGCCGC	GGGATTACCT	
					•	
		AACTATGGAG				
101	GTCAGTCAAT	GAGACTGGGT	CTAGGTGGCA	ACGCACCAGT	TTCCATTCCT	
151	CAACAATCTC	AGTCTGTAAA	GCAGTTACTT	CCAAGTGGAA	ACGGAAGGTC	
201	TTATGGGCTT	GGGTCAGAGC	AGAGGTCCCA	GGCACCAGCA	AGATACTCCC	
251	TGCAGTCTGC	TAATGCCTCT	TCTCTCTCAT	CGGGCCAGTT	AAAGTCTCCT	
301	TCCCTCTCTC	AGTCACAGGC	ATCCAGAGTG	TTAGGTCAGT	CCAGTTCCAA	
351	ACCTGCTGCA	GCTGCCACAG	GCCCTCCCCC	AGGTAACACT	TCCTCAACTC	
401	AAAAGTGGAA	AATATGTACA	ATCTGTAACG	aggaatcact	AGTGCGGCCG	
451	CCTGCAGGTC	GACCATATGG	GAGAGCTCCC	AACGCGTTGG	ATGCATAGCT	
501	TGAGTATTCT	ATAGTGTCAC	CTAAATAGCT	TGGCGTAATC	ATGGTCATAG	
551	CTGTTTCCTG	TGTGAAATTG	TTATCCGCTC	ACAATTCCAC	ACAACATACG	
601	AACCGGAAGC	ATAAAGTGTA	AAGCCTGGGG	TGCCTAATGA	ATGAGCTAAC	
651	TCACATTAAT	TGCGTTGCGC	TCACTGCCCG	CTTTCCAATC	NGGAAACTGT	
701	CGTGCCAACT	GCATTAATGA	ATCGGCCAAC	GCGCGGGGAA	AAGCGGTTTG	
751	CGTATTGGGC	GCTCTTCCGC	TTCCTCGCTC	AATGAATCCC	TGCGCTCNGT	
801	CCTTCCGNTG	CGGNNAACGG	TATCACTCAC	TCNAATT		
ANT	ISENSE					
1	ATNNATATCA	AGCTATGCAT	CCAACGCGTT	GGGAGCTCTC	CCATATGGTC	
51	GACCTGCAGG	CGGCCGCACT	AGTGATTGCT	CGTTACAGAT	tgtagatatt	PRIMER 44
101	TTCCACTTT	GAGTTGAGGA	AGTGTTACCT	GGGGGAGGGC	CTGTGGCAGC	
151	TGCAGCAGGT	TTGGAACTGG	ACTGACCTAA	CACTCTGGAT	GCCTGTGACT	
201	GAGAGAGGGA	AGGAGACTTT	AACTGGCCCG	ATGAGAGAGA	AGAGGCATTA	
251	GCAGACTGCA	GGGAGTATCT	TGCTGGTGCC	TGGGACCTCT	GCTCTGACCC	
301	AAGCCCATAA	GACCTTCCGT	TTCCACTTGG	AAGTAACTGC	TTTACAGACT	
351	GAGATTGTTG	AGGAATGGAA	ACTGGTGCGT	TGCCACCTAG	ACCCAGTCTC	
401	ATTGACTGAC	CAACACTGTA	ACCCTGGCCT	ACAGATTTGA	стсфатастт	-PRIMER 105
451	GTTTTGCTGC	AGGTAATCCC	GCGGCCATGG	CGGCCGGGAG	CATGCGACGT	

FIG. 5B-1.

501 CGGGCCCAAT TCGCCCTATA GTGAGTCGTA TTACAATTCA CTGGCCGTCG
551 TTTTACAACG TCGTGACTGG GAAAACCCTG GCGTTACCCA ACTTAATCCC
601 CTTGCAGCAC ATCCCCCTTT CGCCAGCTGG CGTTAATAAC GAAGAAGCCC
651 GCACCGATCG CCCTTCCCAA CAGTTGCGCA GCCTGAATGG CGAATGGACG
701 CGCCTGTTAG CGCGCATTAA ACCCCGCGGG TGTTGTGGTT ACGCCGCAGC
751 GTGACCGCTA CACTTGCCAC CCCCTAACGC CCGCTCCTTT CCCTTTCTTC
801 CTTCCTTTCT CGCCACGTCC CCCGNTTTCC CCGGTCCAACT CTAAATCGGT

FIG. 5B-2.

	10/31	
20	MSNVHLQQNNYGVKSVGQSYGVGQSVRLGLGGNAPVSIPQQSQSVKQLLP .	50 69
51	SGNGRSFGLGAEQRPPAAARYSLQTAN.TSLPPGQVKSPSVSQSQASRVL	99
70	: :	119
100	GQSSSKPPPAATGPPPSNHCATQKWKICTICNELFPENVYSVHFEKEHKA	149
120	GQSSSKPAAAATGPPPGNTSSTQKWKICTICNELFPENVYSVHFEKEHKA	169
150	EKVPAVANYIMKIHNFTSKCLYCNRYLPTDTLLNHMLIHGLSCPYCRSTF	199
170		219
200	NDVEKMAAHMRMVHIDEEMGPKTDSTLSFDLTLQQGSHTNIHLLVTTYNL	249
220	NDVEKMAAHMRMVHIDEEMGPKTDSTLSFDLTLQQGSHTNIHLLVTTYNL	269
250	RDAPAESVAYHAQNNAPVPPKPQPKVQEKADVPVKSSPQAAVPYKKDVGK	299
270	RDAPAESVAYHAQNNPPVPPKPQPKVQEKADIPVKSSPQAAVPYKKDVGK	319
300	TLCPLCFSILKGPISDALAHHLRERHQVIQTVHPVEKKLTYKCIHCLGVY	349
320	TLCPLCFSILKGPISDALAHHLRERHQVIQTVHPVEKKLTYKCIHCLGVY	369
350	TSNMTASTITLHLVHCRGVGKTQNGQDKTNAPSRLNQSPGLAPVKRTYEQ	399
370	TSNMTASTITLHLVHCRGVGKTQNGQDKTNAPSRLNQSPSLAPVKRTYEQ	419
400	MEFPLLKKRKLEEDADSPSCFEEKPEEPVVLALDPKGHEDDSYEARKSFL	449
420	:: .	469
450	TKYFNKQPYPTRREIEKLAASLWLWKSDIASHFSNKRKKCVRDCEKYKPG	499
470	TKYFNKQPYPTRREIEKLAASLWLWKSDIASHFSNKRKKCVRDCEKYKPG	519
500	VLLGFNMKELNKVKHEMDFDAEWLFENHDEKDSRVNASKTVDKKHNLGKE	549
520	VLLGFNMKELNKVKHEMDFDAEWLFENHDEKDSRVNASKTADKKLNLGKE	569
550	DDSFSDSFEHLEEESNGSGSPFDPVFEVEPKIPSDNLEEPVPKVIPEGAL	599
570		619
600	ESEKLDQKEEEEEEEDGSKYETIHLTEEPAKLMHDASDSEVDQDDVVE	649
620	ESEEKLDQKEDGSKYETIHLTEEPTKLMHNASDSEVDQDDVVE	662
650	WKDGASPSESGPGSQQISDFEDNTCEMKPGTWSDESSQSEDARSSKPAAK	699
663		712
700	KKATVQDDTEQLKWKNSSYGKVEGFWSKDQSQWENASENAERLPNPQIEW	749
713		762

Application No.: 09/107,350
Applicant: Illana Gozes et al.
Tit CTIVITY DEPENDENT NEUROTROPHIC FACTOR ADNF III)
Sheet 11 of 31

750 QNSTIDSEDGEQFDSMTDGVADPMHGSLTGVKLSSQQA 787

FIG. 5C-2.

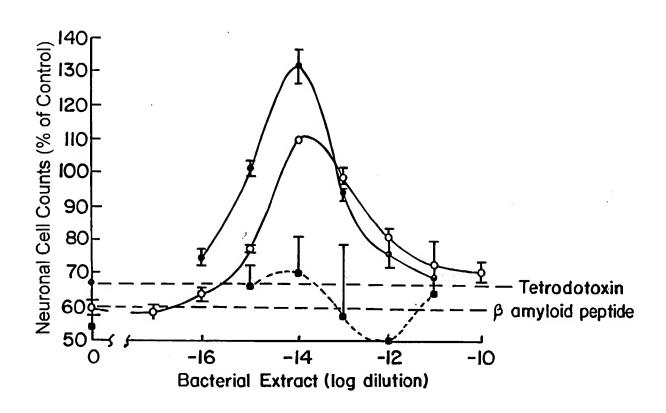


FIG. 6A

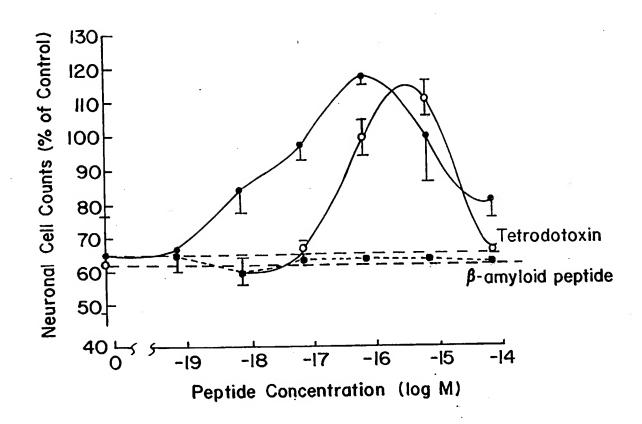
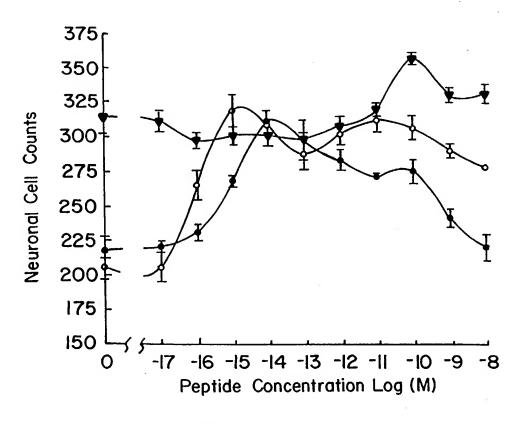


FIG. 6B



- **NMDA**
- gpl20
- Peptide alone

FIG. 6C

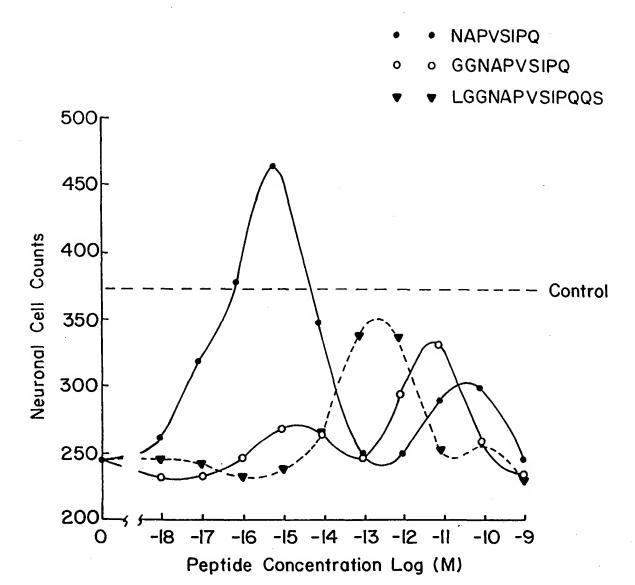


FIG. 7A

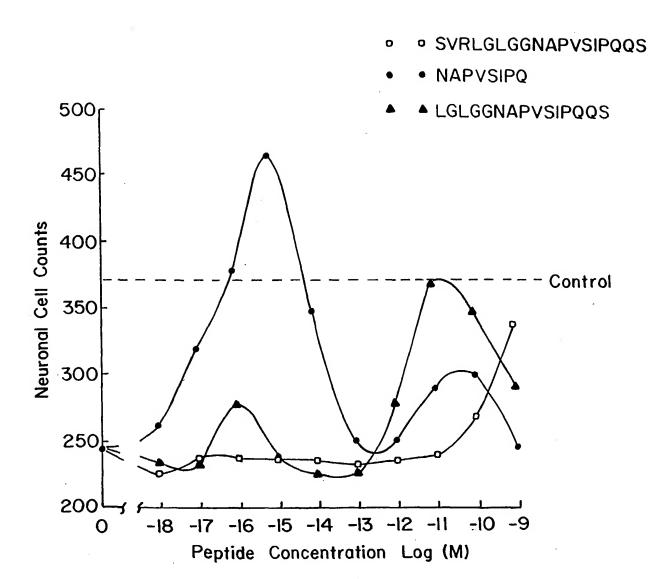
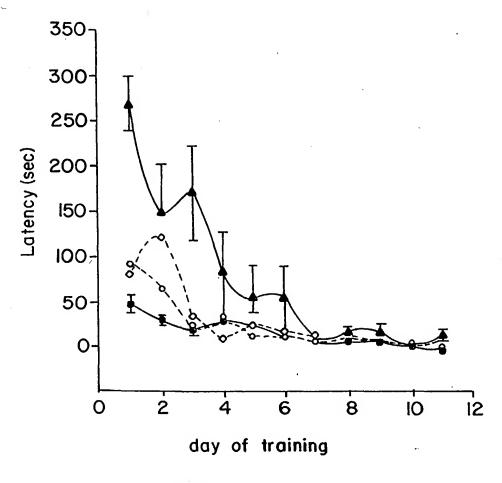


FIG. 7B

The effect of NAPVSIPQ(NAP) on learning and memory



- --e- control
- -- control+NAP
- --- AF-64A
- -- AF-64A+NAP

FIG. 8

E E+N C

SIZE (KB)

ADNP — — — — — — — 5

- 2.1

ACTIN — A A A A

FIG. 9.

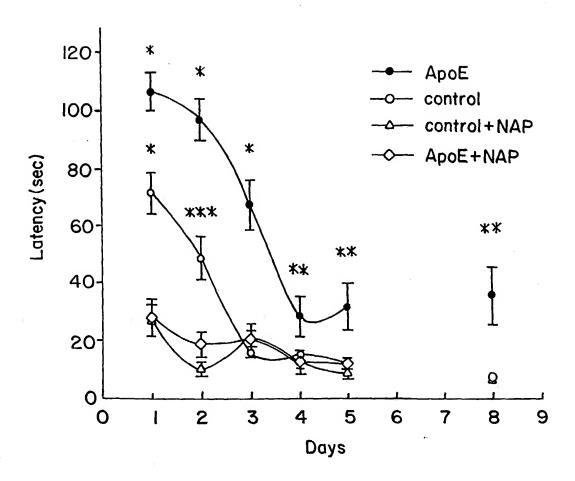


FIG. 10

H	ATGGGACTCCCACCACGAATCAGCTCCCTTGCTTCTGGAAATGTCCGGTCGTTGCCATCACAGCAGATGGTAAACCGATTGTCAATACCAAAGCCCAAC	
100	TAMATICAACGOGAGICAACAIGAIGCEAAGTICACCIGCAGCAAACAACIAIGGAGICAAAICIGIGGGCCAGAGCIAIGGIGITGGCCAGITA	ب ب
•	L N S T G V N M M S N V H L Q Q N N Y G V K S V G Q S Y G V G Q S A	99
777	WRUGERCIEGESTATESTECTORS IN A P V S I P Q Q S V K Q L L P S G N G R S F G S	ω ω
298	recteageagecececageage	
	đ	132
397	ATCTAGAGTATTAGGTC	
	Ot.	165
496	ε	
	c.	198
595	\sim	
	YIMKIH <u>NET</u> SKCLYCNRYLPTDTLLNHMLIHGL 2	231
694	TCTIGICCGIATIGCCGTICCACCTICAAIGAIGIAGAAGAIGGCACACACAIGCGAAIGCITCAIAIIGAIGAAGAGAIGGGGCCIAAAAACGGAI	
	S C P Y C R S T F N D V B K M A A H M R M V H I D B E M G P K T D 2	264
793	TCTACTTTGAGCTTTGATTTGACATTGCAACAGGGCAGTCACCAACATTCATCTCCTGGTGACCACATACAACCTGAGGGATGCCCCGGCTGAATCA	
	STLSFDLTLQQGSHTNIHLLVTTYNLRDAPAES 2	297
892	GITGCTTACCATGCCCCAAAATAATGCCCCCAGTTCCTCCAAAAGCCACAAAACTTCAGGAAAAAAAA	
	V A Y H A Q N N A P V P P K P Q P K V Q E K A D V P V K S S P Q A 3	330
166	GCAGTGCCCTATAAAAAAGATGTTGGGAAGACCCTTTTGCCCTCTTTGCTTTTCAATACTAAAAGGACCCATATCTGATGCACTTGCACATTTACGA	
	сргсғулькартѕраганңгр	363
1090	GAAAGACACCAAGTTATTCAGACAGTTCATCCGGTTGAGAAAAAGCTAACTTACAAATGTATCCATTGCCTTGGTGTGTATACTAGCAACATGACAGCC	
	ERHQVIQTVHPVEKKLTYKCIHCLGVYTS <u>NMT</u> A	396
1189	TCAACCATCACTCTGCATCTAGTCCACTC	
	зтітьнь унс	429
1288	7	
	G L A P V K R T Y E Q M E F P L L K K R K L E E D A D S P S C F E	462
1387	ĸ	
	æ	495
1486	ş	
	K Q P Y P T R R E I E K L A A S L W L W K S D I A S H F S N K R K	528
1585	GTCCGCGACTGTGAAAAGTACAA	
	¥	561
1684	STTTGAAAATCACGATGAGA	
	K D S R V N A S K T V D K K H N L G K E D D S F	594
1783	TAGTTTTGAACATTTGGAAGAAG	
000	S D S F B H L B B B S <u>N G S</u> G S P F D P V F B V B P K I P S D N L 6 gaggaggaggaggaggaggaggaggaggaggaggaggag	627
7007	מאפפאפרכוסואלכיזיטיזיליסייליזייליסייליזייליסייליזייליסייליזייליסייליזייליסייליזייליסייליזייליסייליזייליסייליזייליסייליזייליסייסי	

099		693		726		759		792		825		828	
S	1981 AAATATGAAACTATCCATTTGACTGAGGAACCAGCCAAATTAATGCATGATGCCTCTGATAGTGAGGTAGACCAAGATGATGTGAGTTGAGTGAG	Ω	2080 GGTGCTTCACCATCTGAGAGTGGGCCTGGTTCCCAACAAATCTCAGACTTTGAGGATAATACATGTGAAATGAAACCAGGAACCTGGTCTGATGAGTCT	S	2179 TCCCAGAGTGAAGATGCAAGGAGCAGTAAGCCAGCTGCCAAAAAAAA	>-	2278 GGAAAAGTIGAAGGGTITIGGICCAAGGACCAGICACAGIGGAAAAIGCAICIGAGAAIGCAGAGCGCTIACCAAACCCACAGAITGAGIGGCAGAAI	21	2377 AGCACAATTGACAGTGAGGACGGGGAGCACTTTGACAGCATGACTGAC	S			
b	AA	¥	GAG	回	ΉĊ	တျ	CAG	œ	AGG	ഗ			
Ω	TGG	3	GAT	Ω	'AGT	S	TGG	3	ÖŢĠ	ы			
团	GAG	ш	TCI	S	AAT	z	GAG	ω	AAG	×			
щ	GTT	>	TGG	3	AAG	×	ATT	H	GTG	>			
មា	QTO.	>	ACC	H	TGG	3	CAG	α	GGA	O			
Ø	GAT	Ω	GGA	U	AA	×	S	Д	ACT	H			
Щ	IGA1	Ω	SCC	O.	TI	u	AAC	z	TT	L			
回	SEA	o	NA.	×	SCAG	o	SCC	D.	AGC	S			
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×	I'AG	တ	IAC!	Н	AGA.	Ω	IGC.	Æ,	ű	ሷ			
A LESBKLDQKEEEBBEBEBGGS	TGA,	A K L M H D A S D S E V D Q D D V V E W K D	TAA	O O I S D F E D N T C E M K P G T K S D E S	GCA	A A K K A T V Q D D T E Q L K W K N S S Y	GAA	z	TGA,	DSMTDGVADPMHGSLTGVKLSS			
Ω	CIC	ß	GGA	А	AGT	>	TGA(Ħ	īgĊ.	Ø			
J	TGC	Ø	TGA	ш	TAC	H	ATC	S	AGT	>			
×	TGA	Ω	CTT	Œ	ggĊ	Æ	TGC	A	SSS)	U			
Ø	GCA	H	AGA	Ω	AAA	×	AAA	Z	TGA	Ω			
ß	AAT	Σ	CIC	Ø	AAA	×	GGA	Ø	GAC	H			
ы	ATT	ы	AAT	н	GA	×	GTG	3	CAT	Σ			
H	S	×	ACA	œ	TGC	K	ACA	œ	CAG	ß			
ø	AGC	4	S	ø	AGC	æ	GTC	Ø	TGA				
Ö	S	Д	TIC	ഗ	ည္ဟ	Q,	CCA	œ	CH	<u>CL</u>			
臼	GGA	េ	JGT.	Ö	TAP	×	GGA	Ω	S	œ			
<u>ቤ</u>	TGA	េ	ပ္တင္တ	凸	ŠČAG	ß	Š	×	GGA	Ħ			
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>	AA	H	SAC.	Д	3TG	田	TTG	Ξ	rTG1	Ω	Ö	*	
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E E P V P K V I P E G	PAT	KYETIHLTEEP	3TG(GASPSESGPGS	S	SQSEDARSSKP	SAA	G K V E G F W S K D Q S Q W E N A S E N A E R L P N P Q I E W Q N	3CAC	STIDSEDGEOF	SG	*	
M	7	×	ŏ	Ö	9 T	ß	ğ	Ö	7 A	ഗ	2476 CAGCAAGCCTGA	a	
	198		208		217		227		237		247		

Double Underline - Glycosilation site (amino acid no. 118-120, 205-207, 393-395, 426-428, 576-578, 606-608, 756-758, Single Underline - homologies to HSP60 of ADNP 175-777, 792-794)

Bold + Italic - represents two motifs:

Glutaredoxin active site (amino acid no. 233-243)

2. Zinc finger C2h2 type, domain (amino acid no. 233-254) Bold - potential proteolytic cleavage sites.

Bold + Underline - putative signal peptide

279 345 378 510 543 276 609 246 114 147 180 213 312 411 444 8 81 H M R M V H I D E E M G P K T D S T L S F D L T L Q Q G S H CCATCTCCTGGTAATAATCTGTCCTCCAAAGGAATCCTCCAAAG V H F B K B H K A B K V P A V A N Y I M K I H N F T S K C L Y TCGCTATITACCCACAGATACTCTACATGATGATTCATGGTCTGTCTTGTCCATATTTACCCACATATGATGATGATGATGATGTGGAAAAG R Y L P T D T L L N H M L I H G L S C P Y C R S T F N D V E K Y K K D V G K T L C P TTTAGCTTTAGACCCCAAG COGICITIACCAICACAGCAGAIGGIGAAICGACICICAAIACCAAAGCCIAACIIAAAIICIACAGGAGICAACAIGAIGICCAGIGIICAICIGCAG rgggtcagagcagaggtcccaggcagcaagatactccctg <u>Ta</u>caggccctccccca**ggtaac**acttcctcaaactcaaagtggaaatatgtacaatctgtaatgagctttttcctgaaaatgtc P A A A A T G P P P G <u>N T S</u> S T Q K W K I <u>C T I C N E L F P E N V</u> TATAGTGTGCACTTCGAAAAAAAAAAAAAAAAAAAAGTCCCAGCAGTAGCCAACTACAATTATAAAATACAAATTTTACTAGCAAATGCCTCTAC × Q, ۵, ធា co. Д Σ GCCAGITTATGGTTATGGAAGAGAGTGACATCGCTTCCCATITTAGTAACAAAAGGAAGAAGTGTGTCCGTGATTGTGAAAAGTACAAGCCC × ø ഗ ഗ Д ш ø CTAACAAAGTATTTCAACAACAGCCCTATCCCACCAGGAGAGA Д CGCZ K T Q N G Q D K T N A P S R L <u>N O S</u> P S L A P V K R T CCCTTACTGAAAAAAGGAAAGTTAGATGATGATGATTCACCCAGCTTCTTTGAAGAGACCTGAAGAGCCTGTTGT ccacagecaaaggttcaggaaaaggcagatatccctgtaaaagttcacctcaagctgcagtgccctataaaaaaatgt; Z 凶 z > ø GGAAGATGACAGTTCCTCAGACAGTTTTGAAAA œ Ö z Œ 4 ω S Ω 回 œ I ш Ø, œ Ö P Q P K V Q E K A D I P V K S S P Q A A V P CTTIGCITITCAAICCIAAAGGACCCAIAICIGAIGCACTIGCACAICACITACGAGAGAGGCA ۵ > >ы o а ß Ø Н × ø Ω ß ഗ U Ħ R Y L P T D T L L N H M L I H G L S CGCACACATGCGATGGTTCACATTGATGAAGAGATGGGACCTAAAACAGATTCT A H M R M V H I D E E M G P K T D S > × ជា × × œ Ö α 团 Ø M GTCTGTAAAGCAGTTACTTCCAAGTGGAAACGGAAGGTCTTATGGGCT М z S Σ ഗ ᄓ ഗ Œ ഗ M ß Ö ... 4 Œ >-× Ø Ω ß × z Ω Д v တ Д Ø æ ഗ Ω L O ß × ß × [L យ æ Ω Œ H Ö z I ᆸ ø S **TTCCTATGAAGCCAGGAA** z CTGGGGTTTAACATGAAAGAATTAAATAAAGT Д æ ø S Ö × A, > z Ω × 4 Ö Ω, Ŋ D. × J ᆸ ш S ഗ [--× CAGTCTGCTAATGCCTCTTCT AGTCAA > × ഗ 24 ᆸ TGAAGATGA' Ω × Ö ч Ω A N TGCAGCT Δ 3 ഗ H × ᄓ ø GGTCA ے z 1630 1729 1828 1036 1135 1333 1432 1531 1234 145 244 343 640 739 838 937 442 541

675 708 741 2026 GAGGTTGACCAAGACGATGTTGATGAAGACGGTGCTTCTCCATCTGAGAGTGGGCCTGGATCCCAACAAGTGTCAGACTTTGAGGACAATACC TOCOAAATGAAACCAGGAACCTGGTCTGACGAGTCTTCCCAAAGCGAAGATGCAAGGGGCAGTAAGCCAGCTGCCAAAAAAAGGCTACCATGCAAGG Ω ט Ø W ø Ø Ω Ø Ø O × Ö S Δ 0 × M S Δ 2125 1927 2224

Single underline - homologies to hsp60 of ADNP. Double underline - Glycosilation sites. Bold + Double underline -

Glutaredoxin active site (amino acid no. 234-238) Zinc finger C2h2 type, domains.

- potential proteolic cleavage site. Bold

aaaaccaggactatcggacaaaaccittictgctgcagcgcttgtccattttcctcaaaattcttctgcctacaaaagtcatttccgcaatgtccat

H7 clone

agtgaagactttgaaaatagga*ttctccttaattg*cccctactgtaccttcaatgcagacaaaaagactttggaaacacacattaaaatatttcatgct

24/31

345 180 213 246 279 312 378 147 411 114 15 48 actaacatccatctcctggtaactacatacaatctgaggatgccccagctgaatctgttgcttaccatgcccaaaataatctctccagttcctccaaa <u>AAGCTCACCTACAAATGTATCCATTGGCTTGTGTATACCAGCAACATGACCGCCTCAACTATCACTCTGCATCTAGTTCACTGCAGGGGCGTTGGA</u> PACCATCACAGCAGATGGTGAATCGACTCTCAATACCAAAGCCTAACTTAAATTCTACAGGAGTCAACATGATGTCCAGTGTTCATCTGCAG <u> IGGCCCTCCCCCAGGTAACACTTCCTCAACTCCAAAAGTGGAAAATATGTACAATCTGTAATGAGCTTTTTCCTGÅAAATGTC</u> CAGTGTTGGTCAGTCAATGAGACTGGGTCTAGGTGGCAACGCACCAGTTTCCATTCCTCAA CAGTCTGTAAAGCAGTTACTTCCAAGTGGAAAACGGAAGGTCTTATGGGCTTGGGTCAAGAAGGAGGTCCCAGGCACCAGCAAGATACTCCCTG CTITICCTITICAATCCTAAAAGGACCCATATCTGATGCACTTGCACTTACCAAGAGGCACCAAGTTATTCAGACGGTTCATCCAGTTGAGAAA CCGAACGCCAGCGCAAGTAGCAGCTTCAGCACTTTCAAAGATAAAACCAAAAATGATGGCCTTAAACTTAAGCAGGCTGACAGTGTAGAGCAAGCT atagcaaaggcaggagaaaatcactcaatggggcagtccccttaggctcgaatgcccgagaagagagtagtattcactgcaagcgatgccttttcatg GTTTAITACTGTAAGAAGTGCACTTACCGAGATCCTCTTTATGAAATAGTTAGGAAGCACATTTACAGGGAACATTTTCAGCATGTGGCAGCACCTTAC CTCTCAGTCACAGGCATCCAGAGTGTTAGGTCAGTCCAGTTCCAA doadadagecagataticcctgtaadaagttcacctcaagctgcagtgccctataadadagatgttgggaadacctttgtcct A GACCCAA DA TGGCCAGGA TA A GACAA A TGCA CCCTCT CGGCTTA A TCAGTCT CCAA GTCTGGCA CCTGTGA A GCGCA CTTA CGAGCAA A TGGAA TTT z H ß Ø O ပ ۵, × Ω ഗ o ഗ æ > ß 4 4 [14 J L TATAGTGTGCACTTCGAAAAAAACATAAAGCTGAGAAAGTCCCAGCAGTAGCAACTACATTATGAAAATACACAATTT ω S 4 ႕ Œ H z z z Ω a ഗ O > U I; ט ø z S . H æ > ט н × ഗ Ø U Œ œ တ ۲ × ¥ × ø Д ٦, 0 × 4 ß H Σ Д O U H ø Ø н æ > ч ഗ ᆸ S U H S ø æ œ 14 > z × ტ O ø Ø ß Ø Ŋ Þ z ᆸ 3 CCTABABACAGA Σ Σ Ω Ö H S Þ O z ß × ഗ 0 .1 O H ω œ Ħ > Σ d a o Д × ഗ Ħ × × œ م H Þ а S × × Ö Д Ø М CAGTCTGCTAATGCCTCTTCTCTCATCGGGCCAGTTAAAGTCT a tegecegeacaca tecega tegtitca cattea teaa da batego Ω, ט æ ഗ æ > တ ч Ω ഗ ĸ I J ۵ × တ > Σ O 8 × ß Σ Ω H × M ຜ **>** z J H ω æ а Ω 囟 z ... O 0 ø × z ω H Ø J Δ z ß œ œ S O O CAGAACAACTATGGAGTCAAATCTGTAGG Д × H Ħ 4 z Ö а S I .1 Д Н I Ø O M ರ H ᆸ Д Δ > × ø o Ö H ß TTTACC CCACAGCCAAAGGTTCA > 6 ω Ω, œ ... O S > ч Ĺ > Ö æ Σ ပ္ပ Ŋ ഗ S Ø 1134 1035 1233 540 639 738 837 936 144 243 342 441 45 54

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1332	ខ	CTT	֖֖֖֖֚֭֭֝֝֞֟֝֓֞֝֟֝֟֝֡֡֡֡֡֡֝֓֡֡֡֡֡֡֡֡֡֡֡֡֡֝֡֡֡֡֡֡֡֡֡֡֡֡֡֡֡	SAA	3	ACG.	AAA	GTT	AGA.	TGA	TGA	TAG	TGA	TTC	SCC	AGG	TTC	TII	GAA	GAG	AAG	CCT	3AA(BAGC	Š	TTG	TTT	TAG	CTT	TAG	ACC	CCA	AG	
	Δ	ᆸ	٦,	×	×	æ	×	ы	Ω	Ω	Ω	ഗ	Ω	ഗ	Д	S	[Tr	ſιι	ជា	回	X	<u>-</u> م	<u>പ</u>	ы	•	>	, L	<u>ح</u>	1	Ω	<u>-</u>	×.		47
1431	Ö	TCAT	TGA	AGA.	rga.	TIC	CIA	TGA	ğ	CAG	GAA	AAG	H	TCT	ACC.	LAAC	TAI	TTC	AAC	AAA	CAG	SCC	TAT(CCC	(00)	GGA	GAG	A A	TIG	AGA	AGC	TAG	ď	
	Ö	Ħ	ы	Ω	Ω	S	74	M	K	œ	×	Ŋ	ſщ	H	H	×	>-	ſL,	z	×	a	. م	— ≻ı	L D	μ <u>τ</u> ί	ex ~	⊆	H	Ш	×		A.		51
1530	ပ္ပ	CAGI	H	ATG(TI	ATG	GAA	GAG	IGA(CAT	GGC	TIC	CCA	TIT	TAG	TAAC	AA	AGG	AAG	AAG	TGT	STO	CGT	BATT	GIC	APP	AGT	ACA	AGC	CTG	g	TGT	JG D	
	Æ	တ	.7	3	Ļ	3	×	ß	Δ	н	4	ഗ	ĸ	Œ	ഗ	z	×	24	×	×	Ü	_ >	٠- دع	0	<u>ш</u>	×	×		Δ,	Ö	>			54
1629	ម	3000	3TT.	TAA	PAT	BAA	AGA	ATT	AA	TAA	AGT	GA	gCA.	TGAC	BATC	3 GA1	rrri	GAT	GCT	GAG	TGG(CTA	TTT(BAAR	ATC	ATG	ATG	AGA	AGG	ATT	CCA	GAG	ΤĈ	
	H	Ø	Ŀ	z	Σ	×	យ	H	z	×	>	×	Ħ	缸	Σ	Ω	[Ti	Ω	Ø	Œ	3	۔	<u></u>	<u>~</u>	<u></u>	<u>α</u>	<u>α</u>	×	Δ.	S	ĸ	>		57
1728	Z	TGCI	TAG	TAAC	3AC.	IGC	IGA	CAN	AAA	3CT(CAAK	CCT	TGG	BAAC	3GA.	IGA1	GAC	AGT	TCC	TCA	GAC	₽GT.	TTI	BAAA	ATT	TGG	AAG	AAG	AAT	CCA	ATG	AAA	GT	
	z	Æ	S	×	H	4	Д	×	×	H	z	ı	O	×	臼	A	Ω	S	လ	ທ	ω.	מ	<u>.</u>	<i>1</i> 4	-	<u>ы</u>	E	(ii)	S	Z	ω	S		9
1827	OG	TAGC	S	LIL	TGA (S	TGT	TTT.	IGA.	AGT	TGA	ACC	TAA	PATC	֡֝֝֝֝֟֝֝֟֝֝֟֝֟֝֝֟֝֝֟֝֝֟֝֟֝֟֝֝֟֝֟֝֟֝֟֝֝֟֝	GAAC	GAT	PAC.	CCA	GAA	GAA	CAT	GTA(CTG	AGC.	TAA	TTC	STO DI	AGG	ATG	CHI	CAG	Æ	
	Ö	တ	D,	ſω	Ω	Д	>	Œ,	M	>	M	Д	×	н	S	z	Ω	z	<u>.</u>	ш	ш	T.	>	بد د	ا ح	Η.	Δ,	<u>ш</u>	Ω	a.	co;	<u>ш</u>		64
1926	Ä	TGAG	3GA(BAAC	3CT)	AGA	SC	PAP	AGA.	AGA.	TGG.	TTC	AAA	ATAC	GA.	ACT	CATI	CAT	TIG	ACT	GAG	3AA(CG	ACC P	AAC	TAA	TGC	ACA	ATG	CAT	CTG	ATA	GT	
	တ	ធ	臼	×	ᄓ	Д	ø	×	四	Ω	O	တ	×	×	囟	۲	н	H	ᆸ	⊟	<u>—</u>	េា	۳.	PC,	H	Σ.	Œ	2	æ	S)	Ω	S		67
2025	ğ	GGTI	TGAC	SCA	AGA(CGA	TGT	TGL	IGA(3TG	SAN	AGA	CGG	TGCI	TCI	ຽວວ	עזכז	GAG	AGT	<u>G</u> GG	CCT	3GA	IČČ	SAAC	PAG	TGI	CAG	ACT	TTG	AGG	ACA	ATA	ပ္ပ	
	ш	>	Ω	O	Q	Ω	>	>	凶	X	×	Ω	O	æ	ഗ	д	ß	臼	S	ָ ט	ω Δι	ריז	S	~	~	S	Ω	<u>-</u>	ω.	Д	z	-		70
2124	ŢĞ	CGAZ	MATC	SAA	PCC)	AGG.	AAC	CTG	3TC	IGA(CGA	GTC	TIC	CCAL	AGG	GAZ	\GA1	GCA	AGG	AGC.	AGT	PAG	CCA	3CTG	SCCA	AAA	AAA	AGG	CTA	CCA	TGC	AAG	GT	
	υ	ជា	Σ	¥	а	Ö	۲	3	ഗ	Ω	凹	ഗ	S	ø	S	M	Ω	Ø	œ	S	S	У	<u>α</u>	et.	مد	×	ر بح	. «	E4	Σ.	·	Ö		74
2223	ğ	CAGA	AGAC	3CA(3TT(BAA	ATG	GAA(BAA	TAG	TTC	CTA	TGG,	PAA	GTJ	rga.	AGGC	TTT	TGG	TCL	AAG	3AC	CAG	TCAC	:AG1	GGA	AGA	ATG	CAT	CTG	AGA	ATG	AT	
	a	œ	臼	o	H	×	3	×	z	ß	S	×	Ö	×	>	ជា	O	۲ų	3	ຜ	×	<u>۔</u>	o.	S	<u>ح</u>	~	z	4	Ω	Ξ	z 	<u>α</u>		77
2322	GA	SCG	CTT	ATC	TAA(S	CCA	GAT	TGA	GTG	GCA	GAA	TAG	CAC	AATT	rgac	PAGI	GAG	GAT	GGG	GAA	CAG	TTT	3ACE	AC	TGA	CTG	ATG	GAG	TAG	S. TG	AGC	ပ္ပ	
	ធ	œ	.7	ഗ	z	ρι	o	н	ы	3	α	z	Ø	H	H	Ω	ß	떠	Ω	U	回	O.	L.	<u>۾</u>	<u>~</u>	7	D.	0	>	4	щ	Ω,		80
2421	AT	GCA1	TGG	CAG	CILE	AGC	CGG.	AGT	TAP	ACT	GAG	CAG	CCA	ACAC	392	TA	AGTC	SCCA	GGI	TCC	CTG(BCA	${ m TTG}$	3TG	CAJ	GCI	rgca	GGG	TGG	AAC	TCI	GAT	CŢ	
	Σ	×	U	တ	ı	K	Ø	>	×		S	ß	ø	ø	*																			8
2520 CCAGTGTGACTGCAAAGCTGTCTTCTCACTGGTACTGCCTTGTGAGTACTGGTTGGACTGTGGGGCCATGTGGCCGCTGCAGTTCCAGTGTTTTTTTT	ပ္ပ	AGTC	GTG	ACT	30.2	AAG	CTG	TCT	ĮČĮ.	CAC	TGG	TAC	TGC	CT.	3TG)	AGT?	ACTO	GTI	GGA	CTG	TGĞ	GGC	ATG	Igg	ပ္တ	TGC	CAGI	J.J.C.C	AGI	GGI	TAT	TTC	T'A	
2619		AGTCTATGACAGGACAGGCTGTTC	4TG	ACA	3GA(CAG	GCT	GTT	CII	GCT	TCA	gaa	CCT	TCT	CTG1	ACAC	3ACF	SSO	TAA	CTA	AAT	3TG,	AAA	AACC	:AA:	PAAG	TTGCTTCAGAACCTTCTCTGACAGACACGGTAACTAAATGTGAAAAACCAATAAGCTGGTGACTCATGAATACAC	GTG	ACT	CAT	GAA	TAC	AC	
2718		acgaggaaaagcagaggtttattatctgcc ttttca acatttctttccctctgtgaaatgattggtcagatgtttgagaagtgttaaactaattc	BAA	A.A.G	CAG	AGG	TTT.	ATT	TTA	TCT	gcc	TTT	TCA	ACAS	rtt	TT	וַכככ	TCT	GTG	AAA	TGA'	TTG	GTC,	4GA1	GTC	TTT	GAG	AAG	TGI	TAA	ACT	TAAT	ŢĊ	
2817		acatggtagtgtagggccaacatacaagctaccagtctaatgtgtatagtagactttgggaaaagcgatttttttt	3TA(3TG.	TAG	299	S A	CAT	AC.P.	AGC	TAC	CAG	TCL	AATC	3TG1	rat?	AGT#	IGAC	TTT	GGG	AAA	₽GC(3AT	rttı	TTT	CAI	GTA	TTC	ATT	ĊŢĠ	AAT	AGT	ភិ	
2916		AAATGTATATTTGTACAGTCTTTTAGACCTATTCAAGTGATGCTCATGATCCTGTTACTGTGTGCCCATCATAGATTTCTTTTTTAGTGTTTGCCCTTG	rat)	4TT.	rgT.	ACA	GTC	TLL	TAG	ACC	TAT	ŢĊĀ	AGT	GATC	3CTC	PATC	3A.T.C	CTG	TTA	CTG	TGT(300	CAT(CATA	IGA1	TTC	TTT	ΥΤΤ	TAG	TGT	TGC	CCT	TG	
3015		CTGTGTAATAAACG CTCTATCTAGTTTACCTA GCAAAAGCTCAAAA CTGCGCTAGTATGGACTTTTTGGACAGACTTAGTTTTTGCACATAACCTTGTA	TAA'	TAA	ACG(CIC	TAT	CTA	GIT	TAC	CTA	GCA	AAA	GCT	CAA	AACI	IGCC	CTA	GTA	TGG	ACT	rtt'	TGG	ACAG	ACT	TAG	TTT	TTG	CAC	ATA	ACC	TTC	T.A	
3114 CAATCTTGCAACAGAGGCCAGGTAAGATATATATATCTGGACTCTTGGATTATAGGATTTTTTCTTGGTCTGAATATCCTTGACATTACAGCTGTC	g	ATCI	ľŢĞ	CAA	CAG	AGG	ČC	CCC	ACG	TAA	GAT	ATA	TAT	CTG	3AĊ1	rctk	PTTC	GAT	TAT	'AGG	ATT.	l'TT(CTT	зстс	TGA	ATA	TCC	TTG	ACA	TTA	CAG	CTG	TC	

F/G 13B.

3213 AAAAACAAAAACTGGTATTTCAGATCTGTTTTCGAAATCTTTTAAGCTAAAATCACATGCAAGAATTGACTTTGCAGCTACTAATTTTGACACCTTTT

3510 CTGTATTGTGCTTAATGTAAAAAAAAAAAAAAA

Bold underlined: initiator methionine in the mouse sequence (numbers of nucleic acids and amino acids is according Bold: Putative initiator methionine

to the mouse sequence).

Bold, italic, double underline: polymorphic site

F16. 13C.

Application 190.. 09/107,330
Applicant: Illana Gozes et al.

Title: VITY DEPENDENT NEUROTROPHIC FACTOR III NF II

AATTETTEGE TEATEAGAAA GAGAGCTETT TECCTTCCET ETTEGTCATC
AAGETCTECE TECATTECAA CAGTETCACC TETEGATTCC TETEGTCTGAA
COMMENTARY
COMMENTARY
CATAGTTECH TECACAAAAT GAGGCTTTTC CATAGTTEGT TTETTTTT
AACAAGAAAA TEGAGAGGCT TTTTGTTTGT TTTTTTTTTTTTTTCC
COMMENTARY
COMMENTARY
CAGCCAACAA GTACAACTAG CAATTTTAAA
CAGATTTAGCA AGAACTTGCA CTGAGTTTC ATTTACAGGA GCACAAATAA
AAAATATTTGA TTCAAAAATG CATCTGAGT CTTTTAATTT TTCCTGCAGG
AGAACCTCT AAAAGTCATT GCCTTGCAGA GTTTCTGGGA ATGCCTGGGG
AOI GAGGAGCCTG GAACTTGTAA CTGCTTGCCT TGAGTGGCCT TCTCACTCTG

451 GTTTCTGTTC TGTTTTGTTT CGTTTGTTTT TT

FIG. 14.

Application 100 109/100/300
Applicant: Illana Gozes et al.
Title TIVITY DEPENDENT NEUROTROPHIC FACTOR: DNF III)
Sheet 28 of 31

28/31

	CORTEX	CEREBELLUM	MEDULLA	HIPPOCAMPUS	MIDBRAIN	FONG	KIDNEY	TESTIS	INTESTINE	SPLEEN		Size KB)
ADNP ——— mRNA	N.	运		23	対象	· ·.			•		desembled	5
, ·-							. 					2.1
nRNA	٠.	<u> </u>	}- 3	T)+3	÷	es.	443	***				

F/G. 15.

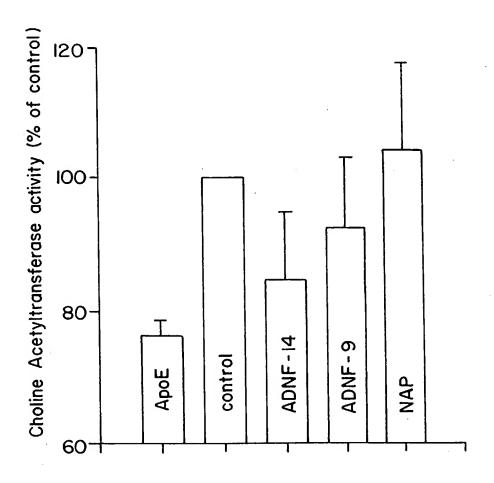


FIG. 16

Placing

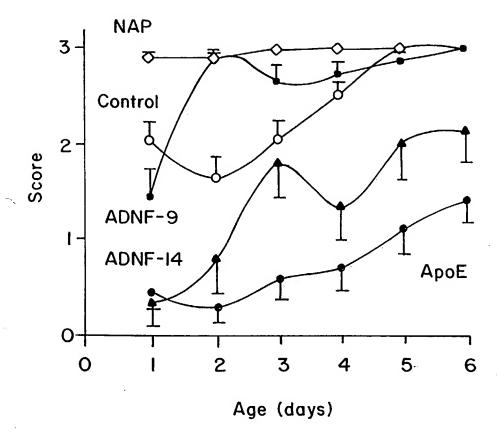


FIG. 17

Application No.: 09/187,330
Applicant: Illana Gozes et al.

itle: IVITY DEPENDENT NEUROTROPHIC FACTOR I. NF III)
Sheet 31 of 31

Poly	morphism			31/31		
нб	clone	GAGTTAAACT	GAGCAGCCAA	CAGGCCTAAG	TGCCAGGTTC	CCTGGCATTG
H10	clone	GAGTTAAACT	GANCANCCAN	CAGGCCTAAG	TGCCAGGTTN	CCTGGCGTTG
H3	clone	GAGTTAAACT	GAGCAGCCAA	CAGGCCTAAG	TGCCAGGTTC	CCTGGCGTTG
H12	clone	GAGTTAAACT	GAGCAGCCAA	CAGGCCTAAG	TGCCAGGTTC	CCTGGCGTTG
H7	clone	GAGTTAAACT	GAGCAGCCAA	CAGGCCTAAG	TGCCAGGTTC	CCTGGCATTG
H4	clone	GAGTTAAACT	GAGCAGCCAA	CAGGCCTAAG	TGCCAGGTTC	CCTGGCGTTG
H2	clone	GAGTTAAACT	GAGCAGCCAA	${\tt CAGGCCTAAG}$	TGCCAGGTTC	CCTGGCATTG

Polymorphic site: $A \rightarrow G$ transition

FIG. 18.